Physical activity: Prescription in health care and relationship to different health measures

Lars Rödjer

From the Department of Molecular and Clinical Medicine

Institute of Medicine at Sahlgrenska Academy

University of Gothenburg Sweden

UNIVERSITY OF GOTHENBURG
2015

'*Vision is the art of seeing what is invisible to others*'
                                    Jonathan Swift

To my family

ABSTRACT

Background: Physical inactivity is one of the major modifiable risk factors, contributing to the global burden of disease. Thus, reducing physical inactivity is of importance for global health. Worldwide, different methods designed to improve physical activity (PA) behaviour in patients, have been developed, including physical activity on prescription (PAP) in Sweden.

Aim: The overall aim of the present thesis was to analyse the association between self-reported leisure time physical activity level and health measures and to study the efficacy of the Swedish method of physical activity on prescription in terms of long-term effects and health-related quality of life (HRQL). Another aim was to analyse health economy and cost-effectiveness of two different variations of the Swedish PAP-method, offering different degrees of support.

The studies included in this thesis offered the opportunity to explore the usability of a single-item question to measure physical activity in different contexts.

Method: Three study populations were included in this thesis. The first study included a random sample of 3,588 adults that answered a questionnaire and collected blood samples. The second study included 3,114 individuals in a working population that received two questionnaires regarding life style, work-related factors and psychosocial health two years apart. In the PAP-study 144 patients and 54 reference patients were included. All received four questionnaires concerning PA and HRQL (SF-36). Cost-effectiveness was estimated from SF-6D derived from SF-36.

Results: The simple physical activity assessment question showed associations with other cardiovascular risk factors and was associated with stress-related mental illness at follow up. Furthermore, there was significant change in the level of PA following PAP at six and 12 months and HRQL, extending to 24 months. The health economic study supported the more supportive framework in this setting, despite being more costly.

Conclusion: The single item question measuring self-reported physical activity level seem to be a valid and feasible tool to assess risk in adults, including working population and patient populations. The efficacy of the Swedish PAP model is further established by the results of the present thesis, showing both long-term effects and cost effectiveness.

Keywords: physical activity, physical inactivity, physical activity on prescription, cost-effectiveness, health-related quality of life, quality-adjusted life year, perceived stress, cardiovascular epidemiology

SAMMANFATTNING PÅ SVENSKA

Bakgrund: Fysisk inaktivitet är en av flera påverkbara riskfaktorer som bidrar till den globala sjukdomsbördan. Alla försök att minska fysisk inaktivitet i befolkningen är av betydelse för hälsan. Det har utvecklats flera olika metoder som syftar till att öka den fysiska aktiviteten hos patienter och i befolkningen. En sådan metod som har utvecklas i Sverige och används inom sjukvården är fysisk aktivitet på recept (FaR®).

Syfte: Det övergripande syftet med denna avhandling var att studera sambandet mellan självrapporterad fysisk aktivitetsnivå och olika hälsomått samt att studera den svenska metoden fysisk aktivitet på recept (FaR®) avseende långtidseffekter och hälso-relaterad livskvalitet. Ett annat syfte var att analysera hälsoekonomi och kostnadseffektivitet för två olika organisationer av den svenska FaR®-modellen.

Studierna i denna avhandling gav möjligheten att studera användbarheten av ett enkelt självskattningsinstrument för den fysiska aktivitetsnivån i olika grupper och sammanhang.

Metod: Tre studiepopulationer användes i denna avhandling. Den första innehöll ett slumpmässigt urval av 3,588 vuxna, som besvarade ett frågeformulär och tog blodprover. Den andra studien innehöll 3,114 vuxna arbetsföra individer som erhöll två frågeformulär som berörde livsstil och arbetsrelaterade frågor samt psykosocial hälsa med 2 års mellanrum. I FaR® studien inkluderades 144 patienter och 54 referens patienter. Samtliga erhöll fyra frågeformulär angående livskvalitet (SF-36) och fysisk aktivitetsnivå. Kostnadseffektivitet beräknades utifrån livskvalitetsdata (SF-6D utifrån svar på SF-36)

Resultat: Fysisk aktivitet mätt med en enkel skattningsskala var kopplad till andra riskfaktorer för hjärt-kärlsjukdom och med stressrelaterad psykisk ohälsa både i tvärsnitt och vid uppföljning. Dessutom fångade skalan en förändring av den fysiska aktivitetsnivån efter FaR® vid sex och 12 månader. Hälso-relaterad livskvalitet ökade också vid 24 månader hos patienter som fick FaR®. Den hälsoekonomiska undersökningen visade att ett mer omfattande stöd kring FaR® kunde motiveras ur ett kostnadseffektivitetsperspektiv.

Slutsats: Den enkla skattningsskalan för självrapporterad fysisk aktivitetsnivå ter sig vara både användbar och giltig för att uppskatta en förhöjd risk hos vuxna, arbetsföra och patienter. Effekten av den svenska FaR®-modellen har ytterligare visats både avseende förbättrad livskvalitet och kostnadseffektivitet på längre sikt.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals. Papers I and II are reprinted with the permission of the publishers.

I   Rödjer L, Jonsdottir IH, Rosengren A, Björck L, Grimby G, Thelle DS, Lappas G, Börjesson M. Self-reported leisure time physical activity: a useful assessment tool in everyday health care.
BMC Public Health. 2012, 12:693.

II   Jonsdottir IH, Rödjer L, Hadzibajramovic E, Börjesson M, Ahlborg G Jr. A prospective study of leisure-time physical activity and mental health in Swedish health care workers and social insurance officers.
Prev Med. 2010, 51(5):373-377.

III   Rödjer L, Jonsdottir IH, Börjesson M. Physical activity on prescription (PAP): long-term effects on self-reported physical activity and quality of life in a Swedish primary care population.
Under revision

IV   Rödjer L, Jonsdottir IH, Börjesson M, Hagberg L. Physical activity on prescription (PAP) in Swedish primary care: cost-effectiveness of two PAP interventions differing in extent and design.
Manuscript

ABBREVIATIONS

ACSM	American College of Sports Medicine
BMI	Body Mass Index
CI	Confidence interval
CRF	Cardiorespiratory fitness
DALY	Disability-adjusted life year
FaR®	Fysisk aktivitet på recept ®
FYSS	Fysisk aktivitet i sjukdomsprevention och sjukdomsbehandling
GPAQ	Global Physical Activity Questionnaire
HADS	Hospitality Anxiety Depression Scale
HDL	High density lipoprotein
HRQL	Health-Related Quality of Life
I	Physically Inactive
ICER	Incremental Cost-Effectiveness Ratios
IPAQ	International Physical Activity Questionnaire
LDL	Low density lipoprotein
LPA	Light physical activity
MCS	Mental component summary
MET	Metabolic equivalent = 3.5 ml O_2 x kg^{-1} x min^{-1}
MID	Minimally important difference
MVPA	Moderate-to-vigorous physical activity
N	Number
NHANES	National Health and Nutrition Examination Study
OR	Odds ratio
PA	Physical activity
PAP	Physical activity on prescription
PCS	Physical component summary
QALY	Quality-adjusted life year
SCORE	Systematic COronary Risk Evaluation
SD	Standard Deviation
SF-36	Short Form 36
SGPALS	Saltin-Grimby Physical Activity Level Scale
SMBQ	Shirom-Melamed Burnout Questionnaire
WHO	World Health Organization

CONTENTS

'*Undoubtedly philosophers are right when they tell us nothing is great or little except by comparison*'

Jonathan Swift, Gulliver´s travels

INTRODUCTION

$\mathcal{T}$he global burden of non-communicable disease is related to lifestyle (1). The different risk factors that account for mortality are unevenly distributed, as can be seen in Figure 1. According to the global burden of disease study 2010, physical inactivity alone accounted for 3.2 million deaths and 69 million life years lost worldwide (2). Furthermore, the global burden of disease attributed to physical inactivity was estimated in 2013 to be 45 million years lost to premature death or reduced quality of life (3). Thus, reducing physical inactivity could have a major impact worldwide.

Deaths attributed to 19 leading risk factors, by country income level, 2004.
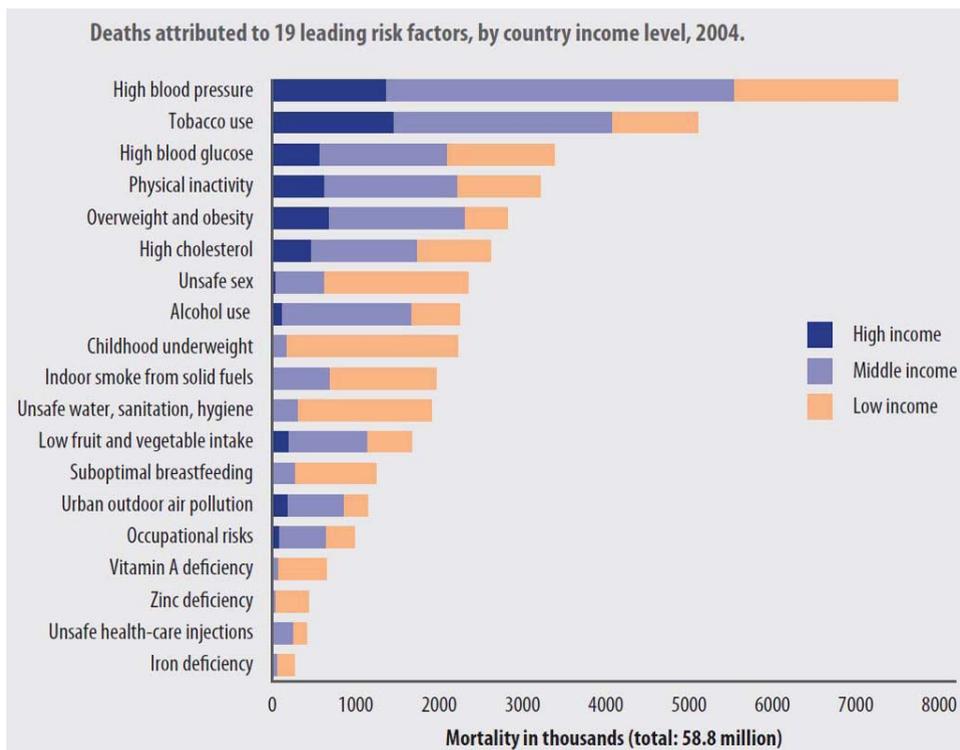
Figure 1. Reprinted with permission from the World Health Organization: Global health risks: mortality and burden of disease attributable to selected major risks, page 10. Copyright © 2009. All rights reserved (1).

The healthcare system is an important arena for promotion of physical activity (4, 5). Regular assessment of physical activity in the healthcare system could possibly both motivate and enhance the use of physical activity as therapy (6, 7).

In Sweden, the guidelines issued by the Swedish National Board of Health and Welfare state that all healthcare personnel should advocate increased physical activity for individuals who are not physically active to a sufficient degree (8). The overall goal for the Swedish healthcare system is for the entire population to be in good health

on equal terms, especially those who are in greatest need (9). Those who have an accumulation of several unhealthy lifestyle habits are amongst those included in this category (10, 11).

A range of methods aimed at increasing physical activity in healthcare have been developed worldwide. In Sweden, the Physical Activity on Prescription (PAP) method was developed in the late 1990s with the aim of using physical activity as a form of therapy (12).

This thesis covers aspects of physical activity and inactivity as factors associated with different health outcomes and as a target for intervention.

Definition of physical activity

The current definition of physical activity (PA) is as follows: 'Any bodily movement produced by the skeletal muscles, leading to increased energy expenditure' (13). Physical activity can be divided into different forms, e.g. occupational, sporting, household and other leisure time activity. Throughout this thesis, PA is used as an abbreviation for leisure time physical activity

Exercise is the part of physical activity that is planned, structured and repetitive and which has the improvement or maintenance of physical fitness as a final or an intermediate objective (13).

The definition of sedentary behaviour is the time spent sitting, lying down and expending very little energy, equivalent to approximately 1.0-1.5 METs (Metabolic Equivalents, 1 MET = 3.5 ml O_2 x kg^{-1} x min^{-1} (14). It can also be defined as less than 100 counts per minute according to an accelerometer (15). In older literature, sedentary was also commonly used to define the lowest level of PA, i.e. including some form of low-level leisure time PA, not just sitting or lying still.

The definition of cardiorespiratory fitness (CRF) is the body's capacity to transport oxygen to the working muscles. Cardiorespiratory fitness is measured in ml O_2 x kg^{-1} x min^{-1}. The limiting step is usually the cardiac capacity to pump blood, although in some cases it may be limited by respiratory capacity, haematological factors (anaemia) and/or peripheral factors in the muscles. Different activities are usually described in absolute intensity terms using the number of METs they are equivalent to. For example, four METs usually corresponds to walking briskly at 6.5 km/h (4 mph) and eight METs corresponds to running at 8 km/h (5 mph) (16). The different MET levels need to be adjusted to take account of the individual's weight when performing body-moving activities.

Historical perspective of physical activity and health

Already, Hippocrates (460-370 BC) wrote about the beneficial effect of PA (17). Hippocrates stated: "Eating alone will not keep a man well; he must also take exercise. Food and exercise, while possessing opposite qualities, work together to produce health." (18). Activities aimed at increasing thermogenesis and weight stability were

mentioned around 400 years BC. In the second century AD, Galen described the many benefits of exercise and his texts were still being used at medical schools during the 18th century (18). The Italian Hieronymus Mercurialis wrote De arte gymnastica in 1569, concluding with the different beneficial effects that can be derived from various physical activities (19). The Swiss physician Samuel Auguste David Tissot (1728-1797) also described the harmful effects of sedentary behaviour and the risks for intellectuals who predominately allow the body to refrain from physical activity. This book was translated into Swedish in 1821 and was entitled 'Råd till de lärde och till dem som föra ett stillasittande levnadssätt' (20).

Still clinically relevant today, Heberden postulated in the 18th century that a case of stable angina pectoris was almost cured by individualised physical activity counselling (21). The individualised activity used at this time was chopping wood for half an hour each day. It should be noted that the intervention was initiated by the patient and not by Heberden. Interestingly, the present physical activity recommendation of at least 30 minutes of moderate intensity PA five days per week (22) was regarded as desirable for health, as early as the 18th century.

Beneficial effects of physical activity

The beneficial effects of physical activity are well described and neatly summarised in the review by Warburton (23). Importantly, PA behaviour can be separated into at least three independent aspects: physical activity level, sedentary behaviour and acquired state, i.e. cardiorespiratory fitness (24). Importantly, beneficial effects can be observed irrespective of the level of cardiorespiratory fitness, as a result of changed physical activity level (25). Furthermore, apart from fitness and physical activity, breaks during sedentary periods of the day have independently positive health effects (24, 26, 27). Consequently, all three of the above-mentioned aspects of physical activity appear to have independent effects (7).

The classical study conducted by Morris et al. of physical activity at the workplace amongst individuals working as bus drivers and conductors in London provided early evidence of the preventative effects of physical activity (28). They presented lower incidence of myocardial infarction among more physically active conductors compared to the bus-drivers. Furthermore, a better three-month survival rate was reported following myocardial infarction amongst conductors compared to the busdrivers (28).

Later, in the Harvard Alumni Health Study by Paffenbarger et al., men who reported higher levels of PA avoided obesity, quit smoking, and maintained normal blood pressure, were independently associated with lower rates of mortality from all causes (29). This study was a prospective observational study with three different follow-ups. The importance of physical activity level in relation to prevention of metabolic disease is also well described (30-37). In two large studies it was shown that an intervention to change diet and physical activity behaviour in pre-diabetic patients decreased the incidence of type II diabetes by 58% (38, 39). In a Chinese prevention study, the reduction in the risk of incidence of type II diabetes was 25-50% for lifestyle intervention compared with controls (40).

Blair et al. showed that for men in the Cooper Clinic Study in Texas, the level of cardiorespiratory fitness was an important predictor for mortality. They stated that those who moved from an unfit state to a more fit state during the study, had a reduced risk ratio than those who remained unfit (41). This finding suggested that those who were unfit should be encouraged to improve their fitness through more physical activity. The later study by Lee et al. concluded that fitness and PA were associated with a lower relative risk of mortality for both genders (42). Fitness was more important and it was suggested that both men and women with a low level of cardiorespiratory fitness should be recommended activities that would help improve their fitness.

Reduced incidence of certain cancers (prostate, breast and colon) has also been described in more active individuals, demonstrating the beneficial effect of physical activity and CRF (43-47) on both incidence and long-term survival after colon cancer diagnosis (48).

With regard to treatment of diabetes, it is possible to improve HbA1c substantially with increased physical activity (49). Furthermore, positive effects on blood pressure can also be achieved amongst a majority of hypertensive individuals (50). The reference book developed for the Swedish PAP method, FYSS (Fysisk aktivitet i sjukdomsprevention och sjukdomsbehandling), states that other conditions, such as mental illness and musculoskeletal, metabolic, pain, pulmonary and neurological disorders, all benefit from increased physical activity (51).

Physical activity and mental health

Physical activity has been associated with effects on different mental health outcomes, such as burnout, perceived stress, anxiety and depression. This has been reported in both cross-sectional and longitudinal studies (52-54). The concept of physical activity as a 'buffer' for psychosocial stress has biochemical correlations, i.e. those being more physically active respond with lower levels of cortisol following stress test and also report better mood and calmness during psychosocial stress testing (55, 56). Furthermore, norepinephrine levels is reduced after a training period when performing the same absolute work load test in healthy subjects (57). This may partly explain the improved mood state during psychosocial stress tests.

Higher cardiorespiratory fitness has been shown to be associated with fewer symptoms of burnout, a higher capacity to cope with stress (58) and a lower incidence of depression (59, 60). Existing evidence has suggested that a high level of physical activity is associated with a lower incidence of depression and anxiety (53). Furthermore, physical activity has been reported to be as effective as regular antidepressants for treatment of depression (61-63). The preventive effects of physical activity with regard to stress-related mental health problems and perceived stress is relatively well studied whereas the importance of physical activity as a treatment is less known (64). Since it has been shown that PA is related to mental health problems, easy methods to assess the level of physical activity in ordinary health care may enable behavioural counselling amongst patients seeking care for mental health problems and possibly contribute to improvement in mental and overall health.

Physical inactivity as a risk factor

The phrase 'factors of risk' was primarily published by the late William Kannel in one of the publications derived from the epidemiological Framingham study (65). The definition of factors of risk was those variables that were suggested to accelerate coronary heart disease, such as cholesterol levels, hypertension and electrocardiographic patterns. In 1963, a parallel epidemiological study in Gothenburg (men born in 1913) was initiated (66). These studies and their sequels contributed to the development of different scoring systems, which included risk factors such as smoking, elevated blood pressure, gender, cholesterol level and diabetes (67, 68), in order to estimate the future risk of cardiovascular mortality. However, while the established risk scores predict future risk, they lack precision, especially at lower risk levels. This is partly due to the fact that these risk scores do not include all the risk factors (heredity, diabetes, sedentary behaviour, physical activity level or fitness). It has been shown that when information about physical fitness is combined with other risk factors this leads to improved risk stratification (69). As reported by several groups (25, 70-72), cardiorespiratory fitness may add important predictive power for future cardiovascular and all-cause mortality and also to regular risk stratification using SCORE (Systematic COronary Risk Evaluation) or Framingham charts (73). However, the most prevalent risk score charts (SCORE, Framingham) still lack information about physical activity level and cardiorespiratory fitness. The addition of physical activity measures could perhaps also promote awareness of which risk factors could be suitable for change. Certain practical barriers contribute to PA not being part of the risk scores. The level of physical activity, for example, is rarely measured in general practice. More recently, it was proposed by Sallis (74) that physical activity should be included as the 'fifth vital sign' in the patients´ medical records. However, easy measures of physical activity are needed that can be used in clinical practice. One example of a risk scoring system that includes CRF is the Cooper Clinic Mortality Risk Index, which requires treadmill tests (75).

Assessment of physical activity

Methods for assessing different physical activity behaviour entities have been developed for clinical and research use. Several methodological aspects need to be considered when physical activity assessment is planned (76). The different tools used can be separated primarily into objective and subjective methods. Furthermore, they can be divided into direct and indirect methods and also in relation to which form of physical activity is being studied. As described by Hagströmer (77), all measures perform differently with regard to validity and reproducibility.

The gold standard for measuring energy expenditure related to physical activity is doubly labelled water. This method has been used to validate other less objective measures. It is expensive and not feasible for large studies. Indirect calorimetry is also valid, although gas exchange analysis can be tedious. Heart rate monitors, accelerometers and pedometers can have advantages but may affect behaviour to a greater extent than self-report questionnaires (77, 78). Diaries and validated questionnaires, such as the International Physical Activity Questionnaire (IPAQ) and the Global Physical Ac-

tivity Questionnaire (GPAQ), can be used to assess leisure time physical activity. The IPAQ is a questionnaire that was presented in Geneva in 1998. It consists of several sets of questions regarding different PA entities – job-related, transportation, housework (domestic activity), recreational and leisure time – together with sedentary/sitting time. IPAQ has been shown to correlate to objective accelerometer among adolescents aged 15-17 but not in younger (79, 80). The IPAQ showed acceptable validity in a Swedish study (81), but IPAQ may have a tendency to over-report. In a review of different self-report questionnaires by van Poppel, the validity and reproducibility of 87 different physical activity assessment tools were analysed (82). Several shortcomings exist, including low correlations between self-reports and objective measures. Furthermore, self-reports also have test-retest difficulties when they include descriptions of different levels of intensity, thus making reproducibility problematic. However, epidemiological studies have usually relied on self-report questionnaires when assessing physical activity behaviour and these have also shown associations with health outcomes independent of what is predicted by fitness (24, 25).

The physical activity performance capacity measured using a cardiorespiratory fitness test is considered to have the strongest predictive validity of the different physical activity entities (42). The fitness level is usually assessed by means of cycle tests (83) or treadmill tests (84) with increasing load. Other tests, such as the Cooper 12-minute run test (85), six-minute walk test (86) and the submaximal Ekblom-Bak test (87), are used. Importantly, CRF can be improved by an increased level of physical activity (88, 89) although it is related to genetic variations and not everyone responds with increased CRF following an exercise period (90, 91), thus making evaluation using CRF tests sometimes insufficient. Importantly, a 'non-responder' to maximal oxygen uptake (VO_2-max) is not related to a lower degree of beneficial effects of PA on other outcome measures (hypertension, diabetes, depression) (92). The cycle test is considered to be one of the best methods for estimating fitness level (83, 87). In addition, the development of a sub-maximal exercise test, such as the Ekblom-Bak test (87), may offer a simple eight-minute test, feasible in regular healthcare. However, the cost of performing one test is still fairly high and it would also require sequential testing. Accelerometers are motion sensors that have been used in research that have shown-independent effects of sedentary behaviour (26, 27, 93, 94). Sedentary behaviour is best assessed using accelerometers (95).

Recently, a combination of different physical activity entities (CRF and accelerometer data) confirmed independent correlations with metabolic syndrome health outcome measures in the SCAPIS pilot study in Sweden (96).

As regards sedentary time, there is no specific recommendation for time spent sitting. Furthermore, it is still unclear how long each break needs to be or how many breaks are needed during sedentary periods to reduce the effects of sitting too much. As regards fitness testing, it could be possible to unintentionally fail to recommend those who are sedentary and yet still highly fit to take breaks during sedentary periods. Even so, those performing physical activity at an increased level but still without improved CRF, could be inhibited due to an absence of a positive response to training.

Depending on the study objective, it is usually important to consider both feasibility, validity and the cost from the clinical perspective. Single-item questions are feasible and valid, especially in larger epidemiological studies, while more objective instruments are preferred for experimental or smaller studies, not least for financial reasons.

Importantly, to the best of our knowledge there is no simple assessment tool that assesses all aspect of physical activity. It is also unclear which PA entity that is the most important for all health outcomes. Cardiorespiratory fitness is possibly the strongest predictor for mortality but low levels of sedentary behaviour and regular daily physical activity of light, moderate and vigorous intensity is also important. Therefore, it could be argued that a short and simple assessment tool may be of particular interest from a clinical perspective. Especially, this may be true when considering the conflict of allocation of resources. The use of accelerometer or fitness tests would therefore not only be time-consuming and expensive, it would possibly divert resources from using methods for behavioural change.

The single-item questionnaire used in this thesis is the Saltin-Grimby Physical Activity Level Scale (SGPALS) (97). It was developed during the 1960s and has been used in epidemiological research in many Scandinavian studies (98-101) and in English-speaking countries (102). The SGPALS instrument has been shown to correlate to fitness level (103-105) and be associated with future mental illness (106, 107), cardiovascular morbidity and mortality (102, 108) and cardiovascular risk factors (109). It has been validated against doubly labelled water and has shown good validity in relation to total energy expenditure (110). However, the concurrent validity compared to objective accelerometer measures has shown to be poor but have predictive validity (111). Furthermore, people tend to overestimate their physical activity, as described recently in a comparison with self-reports and objective measures (112). However, this simple instrument supposedly captures the self-reported mean physical activity behaviour during the past year and the usability of this instrument for different purposes is one of the main aims of this thesis. The instrument includes a four-level description of different physical activity levels. It has been brought up to date and adopted over time.

Recommended level of physical activity in the population

Present physical activity guidelines worldwide (113-115) are largely consistent with the recommendations published in 2010 by the World Health Organization (22). The Swedish Society of Medicine ratified the recommendations stipulated by the Swedish Society of Exercise and Sports Medicine (specifically its section: the Professional Associations for Physical Activity (Yrkesföreningar för Fysisk Aktivitet, YFA) in October 2011, see Box 1 (116). One difference from the WHO guidelines is the inclusion of recommendation on breaks in sedentary behaviour, in the Swedish recommendations. Furthermore, the Swedish National Board of Health and Welfare has published national guidelines that stipulate that all healthcare personnel should recommend increased physical activity to all individuals receiving healthcare who are insufficiently physically active (8).

Physical activity can include recreational activities, such as outdoor recreation, exercise/physical training, sports and gardening, activity at work or home, as well as active transport in everyday life, such as walking and cycling.

To promote health, reduce the risk of chronic diseases, prevent premature death and maintain or improve physical capacity, it is recommended that:

- All adults,18 years and older, are physically active for a total of at least 150 minutes per week. The intensity should be at least moderate. At high intensity, the recommended minimum is 75 minutes per week. Activity of moderate and high intensity can also be combined. The activity should be spread out over several days of the week and recorded for at least 10 minutes.

- The activity should be aerobic in nature, where moderate intensity causes an increase in heart rate and breathing, while high intensity produces a marked increase in heart rate and breathing.

- Examples of physical activity that meet this recommendation are 30 minutes of brisk walking five days per week, 20-30 minutes of running three days per week, or a combination of the two.

- Additional health effects can be achieved by adding a further amount of physical activity. This can be done by increasing the intensity or number of minutes per week, or both.

- Muscle strengthening physical activity should be performed at least twice a week for most of the body's major muscle groups.

-Older people, i.e. adults over 65, should also work out for balance.

-Older people, or individuals with chronic medical conditions or disabilities, who cannot manage the above recommendations, should be as active as their physical condition permits. Pregnant women are advised to take regular physical activity although the choice of activities can be adapted to their condition. In these cases, specific recommendations can be found in FYSS (www.fyss.se), a handbook on physical activity for the prevention and treatment of disease.

- Prolonged sedentary behavior should be avoided. Regular short breaks ('stretch your legs') with some form of muscular activity for a few minutes are recommended for those who have sedentary work or who sit a great deal during their spare time. This also applies to those who meet the above recommendations for physical activity.

Box 1. The Swedish national recommendations on physical activity (116)

The level of physical activity in different populations

Worldwide, the prevalence of physical inactivity is described as a pandemic (117). The global prevalence of inactive behaviour in 2004 was estimated to be 17%, insufficiently active 41%, moderately active 17% and highly active 25% (1). The definitions of the common categories of physical activity behaviour are shown below, derived from the publication by Danaei et al., and are used in the National Health and Nutrition Examination Study (NHANES) (118).

Categories of physical activity are defined below using responses to questions regarding physical activity during the past 30 days.
Inactive, no moderate or vigorous physical activity
Low-active, <2.5 h/week of moderate activity or, <600 MET• min/week
Moderately active, either ≥2.5 h/week of moderate activity or ≥1 h of vigorous activity and ≥600 MET• min/week
Highly active, ≥1 h/week of vigorous activity and ≥1,600 MET• min/week

According to a survey conducted 2011 by WHO, the prevalence of insufficiently physically active adults, was 31% worldwide (119). The definition for insufficiently active in this report was as follows: 'less than five times 30 minutes of moderate activity per week, or less than three times 20 minutes of vigorous activity per week, or equivalent' (119).

In epidemiological research, measurement of the self-reported level of physical activity has been frequently used and this possibly underestimates the true prevalence of inactivity. In Sweden, a yearly telephone interview and survey are conducted – 'Sweden's National Public Health Survey: Health on equal terms'. A random sample of individuals is selected, normally totalling 20,000. The report from 2014 stresses that even though Swedes report a more physically active lifestyle, there is still a large group reporting being physically inactive during leisure time, since 2004 this group has varied between 12-14 percent (120). Importantly, among the individual in the group with short education, more than 20% report the lowest level of physical activity.

The group that reports the highest fulfilment of national guidelines according to the Public Health Agency of Sweden (Folkhälsomyndigheten) is women with a long education (more than 12 years), of whom more than 70% report 'sufficient' physical activity, while less than 10% report physically inactive leisure time (120). In the overall population 62-64% has fulfilled national guidelines since 2004 (measured as self-reported physical activity of at least 30 minutes per day) (120). These figures have been questioned, not least on the basis of the use of a non-validated PA question (121). In contrast, a study from Östergötland, only 25% of the population in 2006 were estimated to being sufficiently physically active according to national guidelines (122).

The shortcomings of self-reports need to be compared with studies using more objective assessments of physical activity in order to improve worldwide monitoring and validity of national and international guidelines. Hence, in a Swedish study using an accelerometer, it was estimated that a mere 6-8% of men and women aged 50-65 ful-

filled the national guideline for physical activity (121). In a study published in 2007 by Hagströmer et al., the fulfilment of physical activity guidelines was 1%. In both these two studies, depending on how the national guidelines are interpreted (123). Furthermore, a longitudinal follow-up of 1,172 participants showed increased sedentary behaviour and reduced average physical activity amongst men and the elderly in Sweden in 2008 compared to 2002, further supporting the concern regarding the physical activity level in the population (124).

Assessment of physical activity is a complex endeavour. The independent effects of sedentary behaviour, regular physical activity and cardiorespiratory fitness are still underappreciated, since many guidelines lack appropriate goals to stress the multidimensional effects related to physical activity (7). If the purpose is to improve behaviour, there is an obvious need to assess it. The use of accelerometers or performing ergometer tests on patients in daily clinical practice is resource demanding. Consequently, depending on the objective, the use of a simple feasible assessment tool is desirable.

Methods for improving physical activity

There is sufficient evidence, to take action against the physical inactivity pandemic on several levels in the society (117, 125, 126) and not least within the healthcare system (4, 5). Many agree that physical inactivity is a worldwide problem and different organisations urge the healthcare system to react (126). American College of Sports Medicine (ACSM), for example, advocates that sports medicine physicians must offer guidance, act as a role model in terms of physical activity and direct patients towards various community resources for training and fitness development (4). Assessment of PA level as a proposed fifth 'vital sign' is carried out by Kaiser Permanente in the US, with the aim of contributing to the willingness among physicians to discuss their patients' lifestyle (74).

Different methods to achieve an increase in PA among patient populations can be found worldwide, showing varying outcomes. Examples of such methods include the Green Prescription in New Zealand, exercise referral schemes in the United Kingdom, Exercise is Medicine in the USA, Training on Prescription in Denmark, Physical Activity on Prescription in Finland, Green Prescription and Healthy Life Prescription in Norway and PAP in Sweden. A review of exercise referral schemes to promote physical activity in adults concluded that 17 inactive/sedentary individuals needed intervention for one individual to reach the recommended physical activity level (127). Another review of observational and randomized controlled trial (RCT) studies – mainly from the UK – dealing with physical activity on prescription, concluded that limited evidence existed for the methods studied (128). They did conclude, however, that a short-term increase in physical activity can be achieved following PA prescription and a reduced level of depression was seen among patients (128). Evidence of the efficacy of the Swedish model of physical activity on prescription, which differ from other PAP schemes, is presented below.

In 2011, the Swedish National Board of Health and Welfare published national guidelines on recommended methods for preventing disease by changing patients' lifestyle

habits (8). Patients who are insufficiently active should be offered individual counselling to improve their physical activity level and should also be offered adjuvant therapy (diaries, prescriptions) and follow-up. They concluded that provision of oral advice only with regard to physical activity is inferior to methods that include prescription, a diary, a pedometer and follow-up. This level of intervention corresponds to the Swedish PAP method, which was developed in the 1990s (12) and later translated into English (51). The FYSS book, collecting the scientific evidence for the health effects of PA, is unique in terms of its comprehensiveness and evidence requirements. Similar books have however, been published elsewhere, including the US (129).

The Swedish physical activity on prescription (PAP) method

The Swedish PAP method includes a written, prescription of physical activity by a healthcare professional. The method is used predominantly in primary care for patients with insufficient levels of physical activity, having a simultaneous medical condition. The method includes five main parts, depending on local routines. The patient-centred perspective is the most central element of the method. This includes factors such as the patient's health status, previous experience of PA and level of habitual PA, limitations and strengths, interest and self-efficacy. The second part is the formal prescription based on the patient-centred interview. The third part is using the book 'Physical activity in the prevention and treatment of disease' (FYSS in Swedish), which summarises evidence-based knowledge regarding physical activity and different diagnoses. The book was first published in 2003 (12) and was updated in 2008. A new update is in progress (2015/2016). It includes recommendations for the type and level of activity for many health conditions. These recommendations should always be individualised for each patient. The physical activity can then be performed outside the health care system either within some public physical activity organisation or be self-monitored. The fourth part of the PAP method therefore includes cooperation with other third-party organisations outside the healthcare system. The fifth part of the PAP method is the stipulated follow-up, which varies considerably due to geographical and local routines. Typically, the patient is referred to a coordinator, who can be based at a training centre, pharmacy or primary healthcare centre. Usually, the PAP coordinator conducts a patient-centred interview, including setting of goals, motivational assessment, guidance, follow-up and reporting back to the prescriber. The Swedish PAP method has been described in depth by Kallings (130).

Several PhD theses have been published on the efficacy of this method in Sweden (122, 131-133). They have analysed different aspects of the PAP method, showing adherence to prescription (122, 131), a positive change in self-reported physical activity level (122, 131, 132), metabolic changes (131), health economy (132), and effects on health–related quality of life (131, 132), mostly at six months follow-up. Studies have also evaluated the difficulties concerning implementation in healthcare (133).

In the county of Östergötland, Leijon performed a large survey of a random sample of the adult population, of whom 11% reported being inactive (122). In addition, one-third of those receiving PAP during 2004 and 2005 reported inactivity at baseline. At the three-month follow-up, approximately 50% reported an increased level of physical activity, as was the case for the 12-month follow-up (134). The prevalence of

inactivity was 17% at three months. The self-reported adherence to PAP was approximately 50% at three and 12 months (135).

The randomized controlled study conducted by Kallings et al., covering 68-year-old men and women (n=101) for six months, showed that improvements in weight, neck circumference, fat mass, cholesterol and HbA1c were more pronounced among those receiving PAP than in the control group (136). Furthermore, an increased level of physical activity was reported at the six-month follow-up in an uncontrolled study of 481 patients receiving PAP (137). In a third study, Kallings reported that two-thirds of 240 patients reported adherence to the prescription (138).

Health-Related Quality of Life (HRQL) and economic evaluation of methods in healthcare

One of the most commonly used measures of HRQL is SF-36, which was first developed in English and translated and validated in Sweden in 1995 (139). The need for intermediate health outcomes is extensive and several others exist (140). SF-36 has been used to evaluate PAP in Sweden (132, 137), and worldwide for evaluation of similar methods (128, 141). In the study by Kallings, HRQL according to SF-36 improved significantly at six months, post-PAP (137).

Health-related quality of life can be improved by physical activity. One review concluded that there was limited evidence for longitudinal studies regarding physical activity and HRQL although strong cross-sectional associations exist (142, 143). Furthermore, the vitality and physical functioning dimensions of HRQL were associated more with physical activity. However, the feasibility of using HRQL instruments in longitudinal research makes health economy analysis possible.

Disability-adjusted life years (DALYs)

The World Health Organization was involved in the development of instruments to rate different risk factors of importance and estimate the contribution of diseases to years lost due to premature death and/or decreased quality of life. This led to the development of a new macro economy field, i.e. health economy. In the project 'Global burden of disease', initiated by the WHO and the World Bank, the DALY assessment tool was developed in the 1990s (144). The measurement includes two aspects of the disease: years lost in relation to an expected lifetime (mean age for death in the region) and loss due to 'years lived with disability'. The estimation of the actual importance of an illness for each individual is not included and instead expert groups have made this estimation. Physical inactivity is estimated to account for approximately five million years lost to disability or premature death in high-income countries (4.1%) (1). In the UK it was estimated that physical inactivity was responsible for 3% of the DALYs and £1.06 billion (total cost £70.2 billion) in direct health care costs in 2002 (145). Previous estimates in the UK published in the 'Game Plan' published by the Prime Minister´s Strategy Unit had estimated that for both indirect and direct costs estimated that the burden was £8.2 billion. In Canada a similar calculation reported that 2.5% of the total cost for health care was related to physical inactivity (146). In 2002 a report

from Bolin, it was estimated that merely 0.3% of the total healthcare expenditure in Sweden was related to inadequate physical activity with a potential loss of 27,000 life years (147).

Quality-adjusted life years (QALYs)

The QALY estimation relies on self-report questionnaires that produce a value between 0 and 1, where 1 means a state of perfect health. When these estimations are multiplied with the time period with a changed quality of life level, a marginal QALY improvement can be calculated after adjusting for baseline level of quality of life (148). This marginal improvement/or decrement is than compared to a control-group or only using baseline values to estimate the effect of an intervention. This calculated value is than replaced with an economic value for how much one QALY is accepted to cost according to different willingness to pay levels (described below)

One important difference between DALY and QALY is that the DALY takes an age factor into consideration as described in Figure 2. This factor is not included in the QALY calculation, meaning that an improved health-related quality of life has the same value independent of age, while a disease that occurs in 25 years of age contribute more to DALY than a disease that occurs at the age of 90 years of age, even if the disease has the same duration at both ages.
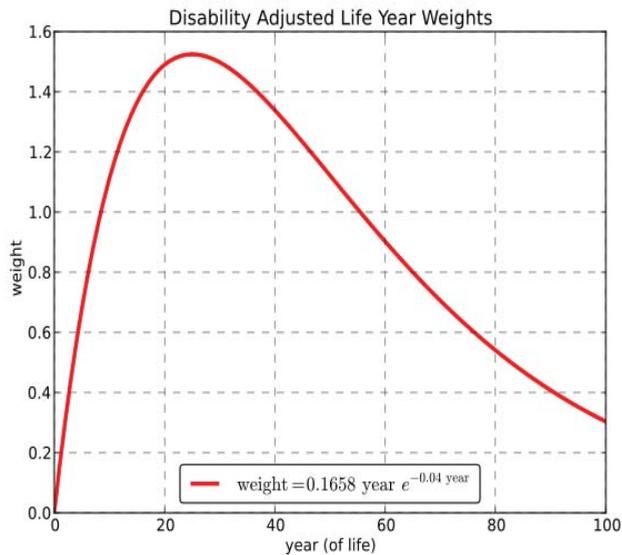
Figure 2. Disability Adjusted Life Year weights in relation to age. (Reproduced from Wikipedia; picture by Martin Strand) (CC BY-SA 3.0).

Willingness to pay

Different methods for estimating the value for one year of perfect health can be performed. Politicians and stakeholders who accept an intervention at a certain cost in order to prolong a life by one year can carry out the estimation. Surveys, asking individuals or patients, to estimate how much they are willing to pay for a medication that gives them one year of perfect health instead of being struck with a serious illness that immediately threatens their life, is another method (149). Worldwide, for example, the cost-effectiveness thresholds for an intervention in the UK are considered to be £20,000-30,000 and in the US, US$ 50-100,000 (149). In Sweden, there is no explicit level, although a threshold of SEK 500,000 has been used (150).

Healthcare stakeholders need cost-effectiveness information for different interventions in order to pinpoint financial support for those interventions that are most likely to generate benefit. One method of evaluating different interventions from an economic perspective is the Net Monetary Benefit method, which includes costs (direct and indirect) and effects in economic terms (148). This means that all effects are converted into monetary units and then compared to all costs related to the intervention. If one intervention is effective, each invested monetary unit generates a quality of life gain or extended life with sustained quality of life. This equation requires a value for each QALY that is estimated using the above-mentioned methods.

Rationale of this thesis

Although few doubt that physical activity is important for good health, it is rarely assessed in general practice and many fail to meet present physical activity guidelines. The possibility of a simple, feasible physical activity assessment tool that can be used in everyday healthcare could possibly improve physical activity counselling. Methods to increase physical activity, such as the Swedish PAP method, have been shown to increase the level of physical activity and HRQL in the short term. We still do not know how PAP works in the long term and this is essential for a successful intervention method. The extent of PAP for optimal cost-effectiveness is also not known.

These aspects have been the prerequisites for this thesis. The aim therefore was to elucidate the self-reported level of physical activity in different contexts using a simple physical activity assessment tool. Furthermore, this assessment tool was used to prospectively evaluate patients receiving PAP and perform a cost-effectiveness analysis of different supportive framework levels surrounding PAP using HRQL methods.

AIMS

The overall aim of the present thesis was to analyse the association between self-reported leisure time physical activity level and health measures and to study the efficacy of the Swedish method of physical activity on prescription in terms of long-term effects and health economy.

Specific aims of Paper I-IV

Paper I   To describe the relationship between self-reported physical activity level and different cardiovascular risk factors in a random sample of Swedish citizens.

Paper II   To analyse the longitudinal effects of self-reported leisure time physical activity in relation to self-reported mental illness, specifically self-reported stress, anxiety, depression and burnout.

Paper III   To evaluate patients receiving physical activity on prescripton (PAP) in primary healthcare during long-term (24 months) follow-up with regard to self-reported physical activity and health-related quality of life.

Paper IV   To analyse the probability of cost-effectiveness at different thresholds of willingness to pay for each gained quality-adjusted life year (QALY), comparing two variants of the Swedish PAP method offering different degrees of support.

MATERIAL AND METHODS

Subjects and study design

The design of studies included in this thesis and a summary of the populations are presented in Table 1 below. A more detailed description of the populations studied can be found in each paper. All the studies were conducted in the Region Västra Götaland, in Sweden.

Table 1. Study design

Paper	Design	Subjects (n)	Women (%)	Men (%)	Age (SD)
I	Cross-sectional	3,588, random sample, adult population	53	47	51 (13) 52 (13)
II	Longitudinal	3,114, random sample, working population	87	13	47 (9.8) 47 (10.7)
III	Observational study, repeated measurement	144 PAP group	74	26	54 (11.3) 56 (11.5)
		54 Reference group	54	46	50 (16.2) 48 (18)
IV	Health economy evaluation of PAP	49 PAP patients, Site I	73	27	56 (9.9) 59 (9.1)
		95 PAP patients, Site II	75	25	53 (11.9) 55 (12.6)

PAP, Physical activity on prescription

Paper I

Paper I was part of the larger INTERGENE (INTERplay between GENEtic susceptibility and environmental factors predisposing to chronic disease) (151) study. INTERGENE included a random sample of individuals aged 25-74 years. Inclusion took place between April 2001 and December 2004. For a further description, see Paper I. The total study population consisted of 3,610 individuals, of whom 1,908 were women (53%). The average age of the responders was 52 years. Data collected consisted of a questionnaire, fasting blood samples and measurements.

Paper II

Paper II was part of a larger longitudinal study, which was conducted during 2004-2006 amongst employees in the healthcare and public service sectors. The overall aim was to investigate different aspects of stress-related health, including burnout, depression, anxiety and the association with work-related environment and lifestyle factors

in the public service sector. The gender composition in this work sector was expected to be skewed. This is reflected in the study sample, which comprised 3,114 individuals, of whom 2,694 were women and 420 were men. The average age at baseline was 47 years. For a detailed description, see Paper II.
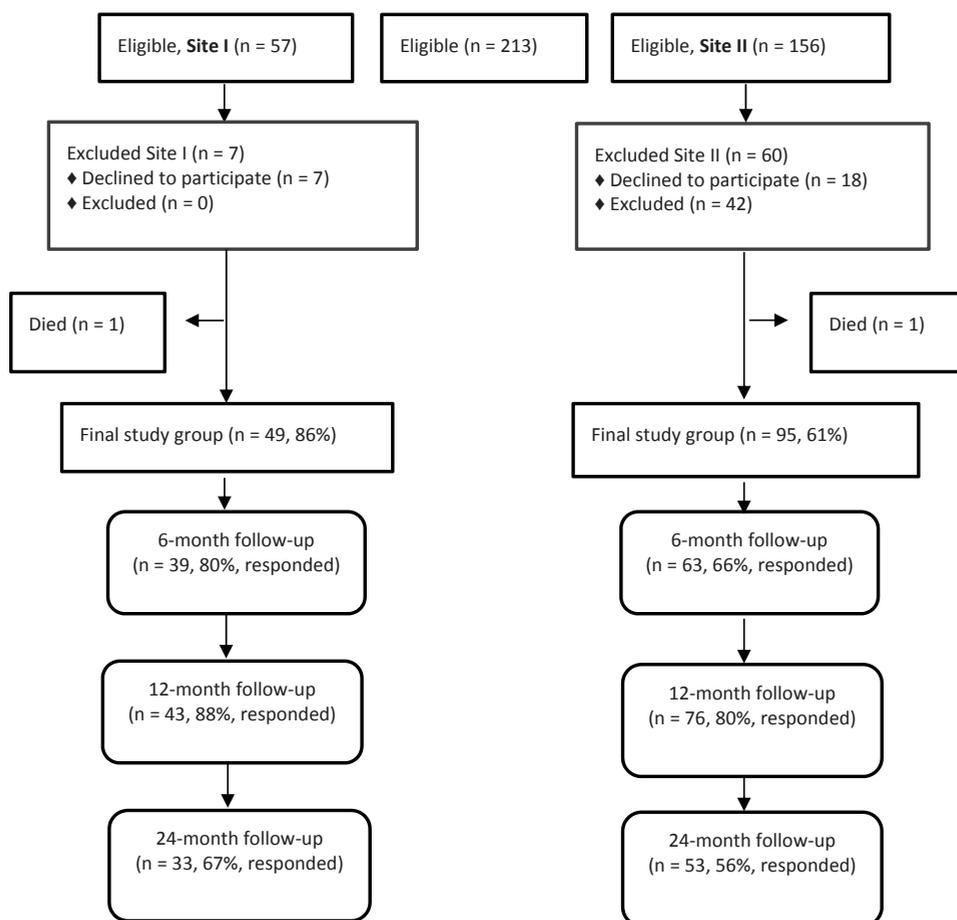
Paper III and IV

Data presented in Paper III and IV is derived from a clinical observational study conducted in ordinary primary care settings. The study group comprised patients receiving PAP at two regional healthcare sites. To be included, they were required to attend a subsequent meeting with the local PAP coordinator. The patients were selected by the prescriber for PAP based on clinical grounds. The prescribers were all authorised personnel working in primary healthcare (physicians, nurses, physiotherapists, dieticians). The written reasons for PAP referral varied considerably for the patients included but all were regarded as insufficiently active. The diagnoses were grouped as follows: musculoskeletal disorders, metabolic disorders (diabetes, cardiovascular disease and overweight), psychiatric disorders and other disorders (which included osteoporosis, asthma, chronic obstructive pulmonary disease, vertigo and cancer). The five exclusion criteria were: prescription of PAP prior to the study, low BMI (<18.5), age (>75 years) and severe disease that could constitute possible barriers to physical activity, i.e. a major stroke or advanced disability and impaired vision or language difficulties. For a detailed description, see Paper III.

The final study group consisted of 144 patients, of whom 52 had a musculoskeletal disorder, 65 had a metabolic disorder, 15 had a mental health problem and 12 had various other reasons, including chronic obstructive pulmonary disease and osteoporosis and inactive behaviour as the reason for referral. The two sites differed with regard to the extent of PAP being delivered. At Site I, the local routine recommended faxing the prescription prior to the meeting with the PAP coordinator. At Site II no such local routine was in place and consequently the total number of prescriptions at Site II during the study period is unknown. The PAP group had a mean age of 55 (SD 11), BMI 30 (SD 5.4) and consisted of 107 women and 37 men. Out of those responding at the 24 months follow-up (n=85), one fourth had a long education (university or similar) and almost 80% lived with someone or were married.

See flowchart page 30.

A reference group was included in the study and consisted of individuals who sought medical care at two other primary care centres located in the same geographical area as the units involved in the study. No attempts were made to influence the level of physical activity in the reference group. The purpose of including this reference group was solely to follow the outcome variables, i.e. self-reported physical activity level and health-related quality of life during the study period, in order to detect any general change over time that might have occurred in a similar primary care population. The study questionnaires and the information letter at inclusion were the only diversions from the usual care for these individuals.

Figure 3. Flowchart, Papers III, IV, modified from Paper III, Rödjer et al.

The reference group consisted of 58 individuals (30 women and 28 men) with a mean age of 49 years (SD 17). They had a significantly lower BMI and were significantly younger compared to the PAP group. The reasons for their health care visits were musculoskeletal disorder, psychiatric condition, cardiovascular disease, infections, blood tests and prophylactic interventions, such as vaccinations. Four patients received PAP during the study period and they were excluded from the analysis. The final reference group thus consisted of 54 patients.

The reference group had a mean age of 49 (SD 17), BMI 27 (SD 5.1) and consisted of 29 women and 25 men. Out of those responding at the 24 months follow-up, one fourth had a long education (university or similar n=36) and almost 70% lived with someone or were married (n=35).

Measures

The different self-report measures used in Paper I-IV are outlined in Table 2 and are described in detail below.

Table 2. An overview of self-reports used in this thesis

	Paper I	Paper II	Paper III	Paper IV
PA assessment	SGPALS	SGPALS, three-month timeframe	SGPALS	SGPALS
HRQL			SF-36	SF-36 and SF-6D
Mental health	Single stress question	SMBQ, HADS and QPS Nordic, single stress question	SF-36	SF-36 and SF-6D

SGPALS, Saltin-Grimby Physical Activity Level Scale, HRQL, Health-Related Quality of Life, SMBQ, Shirom-Melamed Burnout Questionnaire, HADS, Hospital Anxiety and Depression Scale, QPS, Questionnaire Psychological Social, SF-36, Short Form-36

Physical activity level (Paper I-IV)

To assess physical activity, we used the scale developed by Saltin and Grimby (97), which has shown good validity and reliability (35, 110). The SGPALS has been shown to be related to both the CRF level (72, 103, 105, 109) and CVD outcomes (102, 108), Table 3. The moderate and vigorous PA groups were merged to the moderate-to-vigorous PA group (MVPA).

Table 3. Saltin-Grimby Physical Activity Level Scale

"How much do you move and exert yourself physically during your leisure time? If your activity varies greatly between, for example, summer and winter, try to estimate an average. The question refers to the past year."	
1 Physically inactive (**I**)	Almost completely inactive, reading, watching television, watching movies, using computers or doing other sedentary activities, during leisure time.
2 Some light physical activity (**LPA**)	Physically active for at least 4 hours/week, such as riding a bicycle or walking to work, walking with the family, gardening, fishing, table tennis, bowling etc.
3 Regular physical activity and training (moderate PA, **MPA**)	Spending time doing heavy gardening, running, swimming, playing tennis, badminton, calisthenics and similar activities, for at least 2-3 hours/week.
4 Regular hard physical training for competitive sports (vigorous PA, **VPA**)	Spending time running, orienteering, skiing, swimming, playing football, handball etc. several times per week.

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In Paper II, a modified version of the SGPALS was used with a timeframe of three months instead of the original 12 months and with different wording, Table 4.

Table 4. Physical activity levels within a three-month period

"Please tick the option that is closest to how physically active you have been over the past three months"

Inactive, **I**	<u>Mostly sedentary</u>, sometimes walking, light gardening or similar
Light physical activity, **LPA**	<u>Some light physical activity</u> at least for a few hours a week, such as walking or cycling (e.g. to and from work), dancing, normal gardening etc.
Moderate physical activity, **MPA**	<u>Moderate physical activity</u> at least for a few hours a week, such as tennis, swimming, running, gymnastics, cycling (spinning), dancing, football, floorball, heavy gardening or similar
Vigorous PA, **VPA**	<u>Hard exercise regularly</u> and several times a week, at least five hours, where the physical degree of effort is high.

Perceived stress and mental health (Paper I-II)

Different aspects of stress-related mental health symptoms were analysed, using self-report questionnaires. In the first study (Paper I), a single question was used regarding perceived stress, initially developed by Gösta Tibblin and used in the '1913 men study in Gothenburg'. It consists of a statement regarding self-perceived stress, followed by six different levels of perceived occupational and private life stress (152). The stress level is graded on six different levels and the cut-off levels for being defined as stressed are the two highest levels, i.e. constant stress at home or work for at least one year (response 5 or 6). This level of stress has been reported to be related to the incidence of coronary artery disease among men (152) in Gothenburg and the same cut-off was later used in the INTERHEART study (153).

In the second study, (Paper II), self-reported symptoms of depression, anxiety and burnout were measured. For this purpose, the Hospital Anxiety and Depression Scale (HADS) and Shirom-Melamed Burnout Questionnaire (SMBQ) were used (154). The HADS consists of 14 items – seven items related to anxiety and seven related to depression (155, 156). The sum of the scores on each subscale is used to define three different categories – 'non-cases' 0-6, 'possible cases' 7-10, and 'cases' >10. In Paper II we used the >10 as the cut-off point for cases.

SMBQ includes 22 items and four subscales, 'tension', 'burnout', 'listlessness' and 'cognitive failure'. A mean score cut-off level is often used to distinguish cases. Each question/statement can be answered on a seven-point Likert scale, ranging from 1 'almost never' to 7 'almost always'. For the purpose of Study II, we used 4.00 as the cut-off point for defining burnout.

A single question was used to estimate perceived stress in the second study. The question was derived from the QPS Nordic questionnaire (157). The item includes a description of 'stress' and the possible responses are five different levels of stress on a Likert scale, from 'very much' to 'not at all'. The two highest levels were defined

as 'perceived stress' in our study, and the other three options were defined as 'lack of stress'. These two levels have previously been used as cut off for perceived stress (158).

Health-Related Quality of Life (Paper III-IV)

For the evaluation of HRQL, we used the SF-36 questionnaire, which was initially developed in English and later translated into Swedish (139).

Each respondent answers 36 different items. The answers from the respondent are used to calculate different scale scores and to create two different summary scores: PCS (Physical Component Summary) and MCS (Mental Component Summary). Each scale score ranges between the worst case of 0 and the best case of 100. The summary scores have a mean of 50, with a standard deviation of 10 in an average US population, and are more useful for comparing different interventions with the sub-scale scores, which are subject to greater variation.

Small differences observed in HRQL may not be clinically relevant. Recently, a re-view concluded that many studies using SF-36 for outcome measurement report in-sufficient HRQL improvements according to the advocated minimal important dif-ference (MID) (159). A MID of three units in the MCS or PCS score is considered to be a clinically relevant change (160). For subscales, a difference of five is considered clinically relevant.

Health economy (Paper IV)

For the health economy analysis in Study IV, we calculated the health gains and costs, comparing the cost effectiveness of the two different PAP models being evaluated.

Health gain

To analyse the health gain of the PAP intervention, we used changes in HRQL from SF-36 data, converted according to the SF-6D method. This method uses 11 items from SF-36 to estimate a value between 0 and 1, i.e. 1 being perfect health and 0 be-ing equal to death. The method was developed in a British population, with preference scores measured using a standard gamble method (161, 162). We mainly analysed the gained Quality-adjusted life years (QALY) on an individual level using changes in SF-6D between baseline and follow-up. This was done at each follow-up and we assumed a linear effect. The calculation thus conformed to the following line of logic: if the baseline SF-6D were 0.50 and 0.60 at the six-month follow-up, the increment would be 0.1. Due to linearity assumption, this would be divided by 2 as for the cal-culation of a triangle ((0.6-0.5)/2)) = 0.05 QALY gain per year. Since it was only six months, this value would then be divided by 2 (6/12 months) to adjust for a period shorter than one year. For the second year, we included a correction for discount using a three per cent discount rate.

Costs

We considered the costs for the patients and the healthcare system with an intentional societal perspective. We did not include any data concerning changed sick leave, pos-sible prolonged life or changed healthcare consumption. Patients' opportunity costs

for time spent training were not included. We included the prescribers' salaries and assumed a mean time for prescription and follow-up for each profession. The mean cost of the PAP coordinators' time depended on the site being evaluated. The costs for increased physical activity were calculated depending on which site the patient went to and in relation to the reported increase in self-reported level of physical activity. We assumed a stepwise increase in costs derived from the SGPALS level of SEK 500 (physically inactive), SEK 2,000 (LPA), and SEK 3,000 (MVPA) per year. This was discounted for the second year. For missing data related to the self-reported level of PA, we used the last observation carried forward. When data were missing at baseline, we used the lowest level of PA as an option for calculating the marginal increased cost and in doing so we were as conservative as possible and did not underestimate the costs at any time. Although only a few received more than one PAP during the study period, the additional costs resulting from this were included in the analysis.

Cost-effectiveness
The health gain and costs at both sites were calculated. Site I was then compared to Site II using Bootstrap analysis for the costs and health gain on the individual level. The random estimates of 5,000 analyses, comparing the sites and using different levels of willingness to pay per gained QALY, were carried out to make a probability estimate of cost-effectiveness for the sites.

Statistics

The different statistic methods being used in Paper I-IV, are outlined in Table 5, and described in more detail below and in the specific papers.

Table 5. Different statistic methods throughout the studies

	Paper I	Paper II	Paper III	Paper IV
Statistical method	Logistic regression	Cox regression with constant time at risk	T-test for quality of life, marginal homogeneity test for improved PA-level	Net monetary Benefit, Bootstrap analysis, Mann-Whitney U-test, Linear regression
Analyzed variables	Smoking, weight, waist circumference, resting heart rate, levels of fasting plasma-glucose, serum-triglycerides, low-density lipoproteins (LDL), self-reported stress, high-density lipoproteins (HDL)	PA levels in relation to the development of psychosocial self-reported illness	HRQL according to SF-36, SGPALS	HRQL according to SF-6D and societal willingness to pay

Characteristics for groups are presented in the form of means and standard deviations for continuous variables and percent for the categorical variables. Chi-square test was used to analyze group differences at baseline (all papers).

Logistic regression was used to describe associations between physical activity level (as predictor) and other cardiovascular risk factors (Paper I). The highest level of

physical activity (MVPA) was set as reference and for the other levels´ odds ratios was calculated with 95% confidence interval.

Prevalence ratio (PR) with 95% confidence intervals (CI) was calculated for baseline data (Paper II). Cox regression with constant time at risk was used to analyze the associations between physical activity level and incidence of self-reported mental health problems. Those reporting mental health problems at baseline were excluded and physical activity was the predictor in the model. Adjustments for age, gender, body mass index and education was included (Paper II).

Marginal Homogeneity test was performed for evaluation of changed physical activity during follow-up (Paper III and IV). McNemars test was also performed after dichotomising the change in physical activity level as additional analysis (Paper III).

Paired t-test was used for changed health-related quality of life. In Paper III, only complete data was analysed, while imputed values were used in Paper IV. To compare the baseline characteristics of the dropouts and completers, we used a student t-test for numerical data and a chi-square test for categorical data, as we did for a comparison of the reference group versus the PAP group.

Incremental Cost-Effectiveness Ratio (ICER) was calculated for changes in health-related quality of life and costs. In the Bootstrap analysis using all individual data and a random factor between effects and costs comparing Site I against Site II at different thresholds of willingness to pay for QALY was performed too create a probability of cost-effectiveness.

All analyses were performed using SPSS (IBM SPSS Inc., Chicago, Illinois, USA).

RESULTS

Level of physical activity

In the first study, performed in 2001-2004, the self-reported lowest level of physical activity (SGPALS 1) was present in 10% of the population. In the second study, 15% of subjects reported the lowest level of physical activity. In the study of PAP patients (III-IV), the self-reported inactive group made up 32% of the population. The reference group in Paper III reported similar level of inactivity (17%) as the working population in Paper II (15%).

Table 6. Self-reported physical activity at baseline in Studies I-IV according to SGPALS

	n	I (%)	LPA (%)	MVPA (%)	Missing (n)
Study I	3,610	370 (10)	2,263 (63)	955 (27)	22
Study II, Baseline	3,114	457 (15)	1,658 (53)	999 (32)	
Study III, PAP	144	44 (32)	90 (64)	6 (4)	4
Study III, Reference	54	9 (17)	34 (67)	8 (15)	3

I, Physically Inactive, LPA, Light Physical Activity, MVPA, Moderate to Vigorous Physical Activity, PAP, Physical Activity on Prescription.

Physical activity and association with cardiovascular risk factors

In Paper I, the 1,685 men and 1,903 women who were included were stratified according to the self-reported level of physical activity. Logistic regression analysis revealed a clustering of unfavourable cardiovascular risk factors associated with the physically most inactive group (SGPALS 1). The most inactive men had a 5.24 (95% CI: 3.34-8.20) odds ratio (OR) for being a smoker compared to the most active men. In the case of elevated triglycerides and low levels of HDL, an OR of more than 4 was found. For the most inactive (SGPALS 1) women, the OR for smoking was 4.29 (95% CI: 2.82-6.53), for elevated triglycerides 3.28 (95% CI: 2.06-5.22) and for low levels of HDL 2.41 (95% CI: 1.41-4.13). Furthermore, a correlation between the most inactive and a high level of perceived stress was found in men OR 3.59 (95% CI: 2.34-5.49) but not in women.

Physical activity and association with perceived stress and mental health problems

In the second study, consisting of a working population of 3,114 individuals, a higher level of self-reported PA was associated with a lower level of self-reported mental health problems at the two-year follow-up. Those reporting mental illness at baseline were excluded from analysis at the two-year follow-up. A similar negative association was reported for depression, burnout and psychosocial stress (HADS, SMBQ and QPS Nordic question). At baseline and follow up, the most physically inactive (SGPALS 1) individuals, were also more likely to report stress-related illness.

The prevalence of burnout (SMBQ>4.0) at follow-up was 39% among physically inactive individuals at baseline (n=457), and 24% among those who reported being active at the LPA level (n=1,658) and 16% in the most active group, MVPA (n=999), at baseline. The risk reduction of reporting a higher level of PA at baseline was dose-dependent across all the analysed outcome variables at follow-up, including a high level of stress, high burnout, HADS depression and HADS anxiety. The relative risk (RR) for reporting anxiety was not significantly lower for LPA compared with those reporting the lowest level of PA. The RR was adjusted for level of education, gender, BMI and age, which did not alter the associations. Those reporting MVPA at baseline had an adjusted RR of 0.40 (95% CI: 0.27-0.59) for high stress, 0.43 (95% CI: 0.28-0.64) for high burnout, 0.29 (95% CI: 0.15-0.57) for depression and 0.56 (95% CI: 0.34-0.94) for anxiety at the two-year follow up, compared to the initially most inactive group.

Evaluation of PAP

Effects on physical activity level

The 140 patients, who received PAP and answered the SGPALS question, reported a significantly increased level of PA at six months (p<0.001) and at 12 months (p=0.001). At 24 months, there was a non-significant trend for increased PA (p=0.08). Eleven patients remained inactive at 24 months of the 22, who reported SGPALS 1 at baseline, Table 7.

Table 7. Different levels of physical activity at follow-up after PAP (Study III)

	n	I (%)	LPA (%)	MVPA (%)	p-value
Baseline	140	44 (32)	90 (64)	6 (4)	
6 months	99	14 (14)	74 (75)	11 (11)	<0.001
12 months	114	22 (19)	74 (65)	18 (16)	0.001
24 months	84	18 (21)	56 (67)	10 (12)	0.08

I, Physically Inactive, LPA, Light Physical Activity, MVPA, Moderate to Vigorous Physical Activity. The p-value is the Marginal Homogeneity Test for changed PA level at follow-up compared to baseline.

Effects on Health-Related Quality of Life

Health-related quality of life, as assessed using SF-36, indicated a significant change during the study in four of the subscales and in the physical component summary (Table 9, only baseline and 24 months presented) at six, 12 and 24 months respectively when analysing all patients (n=144 at baseline).

Significant improvements were seen for physical role limitation, bodily pain, general health, vitality and PCS scores. The p-value for physical functioning was 0.08. The changes in all four scale scores exceed five points MID (minimal important difference). When only those subjects who completed the 24-month questionnaire were

analysed, changes in general health and vitality also exceeded five points. The change in the physical component summary score exceeded three points in both analyses. At six and twelve months the same scale scores were improved at similar levels. At six months social functioning and physical functioning were also significantly improved and at 12 months mental health was improved as well as the other four. When all the missing values were included using SF-36 manual recommendations, the same scale scores and physical functioning were improved and no significant decrease in SF-36 scale scores was present (data not shown). However, the difference in completers and those lost to follow-up mitigated the overall result, bringing the decrease in two scale scores to below five points (general health and vitality).

When analysing the sites separately, the improvements at Site I were only significant for social functioning, while Site II had significant improvements for physical functioning, physical role limitation, bodily pain and general health at 24 months.

Table 8. Health-Related Quality of Life scores at Baseline (0 months) and 24 months post-PAP according to SF-36 (Study III).

SF-36	0 m	24 m	n	p-value	Mean change	95% CI Lower	Upper
Physical functioning	70.4	74.1	82	.080	3.7	-0.5	7.8
Role limitation, physical	45.6	59.6	80	.001	14	5.6	22.3
Bodily pain	47.8	57.0	83	.002	9.3	3.6	14.9
General health	55.4	61.1	84	.003	5.7	2	9.3
Vitality	51.7	56.8	84	.028	5.1	0.5	9.6
Social functioning	74.6	79.6	85	.105	5	-1.1	11.1
Role limitation, emotional	68.8	76.7	80	.115	7.9	-2	17.8
Mental health	72.7	73.2	85	.779	0.5	-3.2	4.2
Physical component summary	37.5	41.3	76	.002	3.8	1.5	6.1
Mental component summary	46.9	48.2	76	.314	1.4	-1.3	4.1

P-values are T-Test compared with baseline values. CI, Confidence Interval.

Cost-effectiveness

When analysing the difference between the two sites coordinating PAP, there was a clear difference in SF-6D. At Site I, the mean SF-6D was 0.64 at baseline and this level persisted throughout the study. At Site II, the baseline value of SF-6D was 0.56 and at 24 months it was 0.61. This increase in SF-6D was equal to a mean QALY gain at Site I of 0.008 and at Site II 0.071. The costs also differed between sites, the approximated mean cost per patient at Site I being SEK 1,831 (SD 1,295) and at Site II SEK 3,987 (SD 1,720).

The Bootstrap analysis, at a willingness to pay level of SEK 400,000, showed that the probability for the more supportive site (II) of being more cost-effective was 98%. When reducing the effect size related to the prescription by subtracting two-thirds of the mean difference between the sites and increasing the costs by 50%, the probability of cost-effectiveness for the more costly Site II was still 75% (Table 9).

Table 9. Cost-effectiveness at 24 months, mean costs, gain and ICER comparing Site II vs Site I

	24 months
Acquired QALY (95% CI)	0.063 (0.014-0.112)
Mean incremental intervention cost	2156
ICER	34,392
ICER if 33% of QALY gain is related to PAP	103,168
ICER in the case of 33% QALY gain and 50% increased expenditure	198,576

All costs are presented as SEK, ICER, incremental cost-effectiveness ratio SEK/QALY, PAP, physical activity on prescription, CI, confidence interval, QALY, quality-adjusted life year.

DISCUSSION

Paper I-IV included in this thesis has offered the possibility of exploring the use of self-reported physical activity level according to the Saltin-Grimby Physical Activity Level Scale (SGPALS) in several different settings. The first study describes cross-sectional associations between PA levels and established cardiovascular risk factors. The results show that several unfavourable cardiovascular risk factors are higher amongst those reporting lower levels of physical activity. Moreover, a cross-sectional association between lower levels of physical activity and a higher prevalence of self-reported mental health problems was noted in the second study. In the same study, a longitudinal relationship was found between lower incidences of self-reported mental health problems and reporting higher levels of physical activity at baseline.

The other main objective of the present thesis was to explore a method for increasing the physical activity level of the patient, namely physical activity on prescription (PAP). The evaluation of PAP (Paper III and IV) showed long-term effects on the level of physical activity (at 12 months) and health-related quality of life (at 24 months). In a health economic analysis, the more extensive PAP framework showed a high probability of cost-effectiveness compared to a less extensive PAP model.

Physical activity and cardiovascular risk factors

In this thesis we show that the self-reported level of physical activity according to SGPALS is negatively related to major cardiovascular risk factors. Similar results, using various physical activity assessment methods, have been found in Europe (35, 104), and the US: Harvard Alumni Study (163, 164), and the Aerobics Center Longitudinal Study (165). Consistent evidence regarding the level of physical activity and its association with other modifiable risk factors is important. A recent study showed that a simple query regarding PA had additional risk-predicting power for CRF classification (166). Independent effects of physical activity entities have been emphasised in recent years by Bouchard et al. (7) and others (96). In the recent analysis of the global burden of disease, the theoretical minimum risk exposure level for physical activity was set at >8,000 MET minutes per week, i.e. those who report a lifestyle marked by a high level of physical activity (3). A recent Swedish study reported that only seven per cent achieved recommended level of physical activity measured with accelerometer (121). Furthermore, the use of MET minutes per week may not be feasible in clinical practice. The use of a simple one-question PA assessment tool such as SGPALS may be an alternative for simple assessment of PA levels in healthcare.

In Sweden, it is reported that only 25% of the patients recall that they discussed PA behaviour at their last healthcare visit (167). In contrast, 90% of Swedish patients reported that they would prefer to discuss different lifestyle factors when in contact with the healthcare system (168). From the healthcare staff's perspective it has been suggested that 60% of the visits could benefit from discussing lifestyle (169). Both patients and healthcare staff may benefit from the use of SGPALS in clinical practice whenever it is suitable to discuss the level of physical activity in addition to discussing smoking and other modifiable risk factors.

Physical activity and mental health

We also show that the level of physical activity is negatively associated with perceived stress and symptoms of mental health problems (depression, burnout, and anxiety) in both cross-sectional and longitudinal settings. The cross-sectional analysis specifically showed associations between higher levels of self-reported physical activity and self-reported symptoms of mental health problems at baseline. Similar findings have been reported by others (53, 54, 170), and the association between physical activity and depression is well established (62, 63, 171). However, the relationship between physical activity and burnout has yet to be explored extensively.

Although it has been stated previously that physical activity is a 'buffer' for life stress (172), further validation is needed. Our finding supports this theory, reporting in a longitudinal study (two-year follow-up) of a working population (106) an inverse relationship between PA levels at baseline and depression, perceived stress, burnout and to some extent anxiety.

The costs of mental health problems in society are considerable. Existing evidence supports the assertion that physical activity behaviour can improve mental health in different contexts. We have described the relevance of using one simple assessment tool in a working population, indicating the protective effects of higher levels of physical activity. We therefore suggest that SGPALS could be recommended for use in clinical practice when meeting patients and individuals in both a regular and occupational healthcare setting. Our results also demonstrate the potential for increasing the level of physical activity as a means of, in theory, decreasing the risk of developing stress-related mental health disorders. However, these results must be interpreted cautiously, since causality has not been shown.

Evaluation of physical activity on prescription

According to the results in Study III, patients receiving physical activity on prescription (PAP) in a standard primary healthcare setting increase their self-reported level of physical activity by up to at least 12 months. As regards health-related quality of life, there were significant improvements after PAP, even at the 24-month follow-up. Those who responded with an increased level of physical activity at 24 months according to SGPALS, or who reported being MVPA at baseline, improved their Mental Component Summary and Physical Component Summary score by six points at the 24-month follow-up compared to baseline.

These findings confirm the findings in previous reports on the efficacy of the Swedish PAP method with regard to changed HRQL (137) and level of physical activity (134, 137). Other studies that examined the prescription of exercise to improve health-related quality of life have produced similar results (141, 173, 174). However, not all studies support the efficacy of similar 'PAP-like' methods (128). In a study by Myers et al., a nine-month exercise study with four different randomized groups (control, resistance training, aerobic training (or a combination of resistance and aerobic) for diabetic patients showed an improved SF-36 PCS score of two points in the aerobic training group, while the control group score fell by three points (173). In patients

with musculoskeletal disorders, the improvement after initiation of physical activity counselling was similar to our results for HRQL when analysing those reporting musculosceletal pain disorders as a reason for referral (175). Importantly, the Swedish PAP method, as studied in this thesis, differs from the various methods used internationally and comparison of efficacy between methods that have been published (176, 177) may therefore be difficult.

Our results also extend to previous reports, showing the beneficial (short-term) effects of the Swedish PAP method on physical activity level and HRQL (137) by showing a long-lasting effect for up to two years. Furthermore, the results indicate that more support might be needed for some patients to achieve an improved HRQL and to become more physically active. The SGPALS question could possibly be used to broach the topic of physical activity with the patient and to aid actual prescription of PAP and at the same time be a feasible follow-up tool. The use of SGPALS and PAP is supported by the recommendations in the national guidelines, advocating that all healthcare personnel should play an take active part in the behavioural change process of those who are insufficiently physically active and who seek healthcare to improve their overall health (8).

Health economic evaluation of physical activity on prescription

In the final study, we compared two supportive PAP frameworks at two different healthcare sites, showing a high probability of cost-effectiveness for the more extensive PAP variant (high-cost site). The additional cost per gained QALY at the high-support site was approximately SEK 37,000. It has been suggested that more studies are needed to confirm which level of support can still be regarded as cost-effective (178). In the review by Lin et al., it is stated that there is a lack of studies describing how different levels of support affect health outcomes, including HRQL studies (178). In Sweden, one such study by Romé et al. concluded that a low-cost site was more cost-effective than a high-cost site (132). This can be explained in part by the equal improvements in HRQL found at both sites with a small advantage for the low-cost site. The costs per gained QALY (ICER, Incremental Cost Effectiveness Ratio) at the different sites ranged from SEK 200,000-300,000, which is similar to the figures arrived at in our studies using a sensitivity analysis with increased costs and reduced effect size. In our study, using the most conservative approach, the ICER was approximately SEK 300,000, which has been the unofficial level of 'willingness to pay' for a new pharmaceutical drug when introduced onto the Swedish market (179).

In the Green Prescription analysis in New Zealand, they report an improved number of patients meeting PA recommendation levels and improved HRQL after PAP (141). They conclude that prescription of exercise increased the level of physical activity and health-related quality of life. A prior analysis estimated a cost of approximately EUR 965 per gained QALY (< SEK 10,000, 2006 exchange rate) (180). Other interventions for increasing physical activity have revealed costs for improving physical activity level or gaining one QALY ranging from EUR 348 to EUR 86,877, as outlined in the review by Garrett et al. (181). In the UK, recent recommendations concerning Exercise Referral Schemes (182) were published by the National Institute for Health and

Care Excellence (NICE). It states that being physically inactive or being sedentary is not recommended as the sole reason for referral, since cost-effectiveness is questioned for those without an accompanying diagnosis. This further implies a need for more research concerning different levels of supportive frameworks for individuals and patients in need of behavioural change.

In our study, those who reported an increased level of physical activity (increased SGPALS) after PAP also improved their HRQL significantly. This finding supports the recommendation of using SGPALS as an assessment tool during follow-up after PAP, since those reporting higher levels of PA are likely to gain more HRQL.

From an ethical perspective, it is important to use our common societal resources where they achieve the greatest benefit. This cost-benefit principle is one important aspect for the healthcare system to consider. In this respect, the results of the current study add knowledge concerning cost-effectiveness and efficacy of the PAP-method and where necessary may aid the implementation of national guidelines (8) .

Methodological consideration

Several aspects associated with the self-reporting instruments used in this thesis need to be considered. Firstly, the phenomenon of social desirability accompanies behaviours that are commonly regarded as recommendable (183). This typically leads to over-reporting of the true behaviour, in particular the level of PA. Social desirability may thus lead to underestimation of the magnitude of the inactivity problem. Nevertheless, the concurrent and predictive validity of SGPALS has been shown repeatedly, including in relation to fitness and cardiovascular disease. Furthermore, this instrument has been widely used and is currently being employed to assess more than 600,000 individuals (111, 184). SGPALS has the advantage that the staging may also be used as an educational tool, e.g. to demonstrate the gain from substituting LPA for the more vigorous MVPA, which has been shown to be related to level of fitness (103-105). Furthermore, using self-reports in large-scale studies is advantageous from a feasibility perspective and from an economic perspective, i.e. it is easier and cheaper. In this thesis, using extensive and more objective assessments would possibly have affected the results to a greater extent, since by measuring and assessing behaviour it is affected. A minimally invasive assessment was therefore chosen, recognising all the inherent shortcomings of this method (78).

To further analyse the effects of changes following PAP, we included self-assessment of HRQL. Our reference group differed substantially from the PAP group, thus compromising comparisons. Importantly, the use of HRQL as an outcome measure allows a comparison to be made with other control groups in similar settings.

There was a substantial drop-out rate in the various studies, which needs to be taken into account when interpreting the results. In the INTERGENE study (Paper I), the response rate was 42%. This has been presented earlier by Strandhagen et al., reporting that participants were more likely to be women of Nordic origin who were married, and with a higher level of education and a high income, (185). In the second study,

the response rate at baseline was 62% and at follow-up 84%. Finally, in the PAP study (Paper III-IV) the response rate was 60% at 24 months. This was handled using the last observation carried forward method, which is a conservative approach.

There was also a selection bias, as those receiving PAP may to a certain extent be in a group selected by the prescribers. All were included consecutively downstream to the selection by the prescriber as part of clinical practice, and the selection process was thus outside the control of the research group. Furthermore, we had a skewed gender composition, with almost three-fourth of the patients included being women. Similar findings have been reported in previous studies of the Swedish PAP method.

The health economic analysis performed using QALY also has shortcomings that need to be mentioned. Usually, a total societal perspective is advocated. We did not have data for all healthcare costs or for sick leave, which could have been used to describe the economic impact in even more detail. Similarly, we had no access to the exact costs for all activities performed. We did not include any theoretical economic benefit from the reported change in physical activity. This was done by others, who relied on other, often more vague, assumptions compared to HRQL data (186). To counteract these shortcomings, we included a sensitivity analysis to account for any putatively increased costs and we took into account a reduced effect size, which meant that the conclusion was based on a more conservative scenario.

CLINICAL IMPLICATIONS

It has been reported repeatedly that physical activity level is of major importance for overall health. This presents a considerable challenge for the healthcare system, since the overall level of physical activity in the population is low (121) and fitness levels have decreased (187).

Adults at the age of 25 who are sedentary can expect a loss of seven QALYs due to physical inactivity (11). A feasible assessment tool for physical activity behaviour could thus be very useful in everyday healthcare. We show that by studying the single-question self-assessment SGPALS, we could identify associations in various populations between the PA level and several health outcomes, indicating the potential clinical use of this simple tool for identifying patients at risk in different healthcare settings.

There is a considerable need for methods to improve physical activity behaviour. Our study of the Swedish PAP method answers some important questions. This is the first study with a long-term follow-up – two years – thus extending previous reports and providing further support for the efficacy of the PAP method.

Secondly, as outlined in the review by Lin, it is important to explore how costly interventions can be and yet still be regarded as cost-effective (178). Our health economic analysis indicates that a more supportive and costly PAP framework should possibly be advocated. New interventions and treatments require health economic analysis before being launched if society is to spend its money wisely and rule out inefficient methods (188). In addition, Danish studies have concluded that individuals who alter a number of unhealthy habits during adulthood might gain more than eight years' added lifetime per person (189).

By demonstrating the long-term efficacy of the Swedish PAP model (Paper III), as well as showing the cost-effectiveness of a more supportive PAP model (Paper IV), healthcare administrators and practitioners now have added scientific background to support the continued implementation of physical activity on prescription in healthcare. The regular use in healthcare of the combination of SGPALS (for assessment) and PAP (for treatment), certainly has significant clinical potential. We report SGPALS being associated with known cardiovascular risk factors, mental health outcomes and the use of SGPALS for supporting the PAP method in terms of targeting those in need of behavioural counselling. The use of SGPALS as a follow-up measure and as input in the behavioural discussion falls outside the context of this thesis and requires further study.

Importantly, the most physically inactive individuals have the most to gain. Increasing the PA level in this group by a mere 15-29 minutes of physical activity per day has been reported to be the best health trade-off (190, 191). However, all patients who are insufficiently active but do not reach the 8,000 MET minutes per week level still benefit from increasing their PA levels (3), showing the vast potential for improving PA in the population in general and among patients in particular.

CONCLUSION

- There is support for SGPALS as a suitable assessment tool for physical activity behaviour and to identify inactive populations. Unfavourable cardiovascular risk markers are more prevalent among physically inactive adults (Paper I). The most physically inactive individuals – self-assessed as SGPALS 1 – run a particularly high risk.

- Longitudinal evidence supports that those who are more physically active at baseline according to SGPALS were less likely to report stress-related problems (depression, anxiety and burnout syndrome), at the two-year follow-up (Paper II). In addition, inactive men reported more stress than those who were more active.

- Physical activity on prescription (PAP) in primary care improves the self-reported PA level significantly up to 12 months and health-related quality of life parameters up to 24 months (Paper III).

- By using QALY estimations we could conclude that a more supportive and costly framework of PAP was cost-effective (Paper IV). By employing a conservative approach, the incremental cost-effectiveness ratio (ICER) was found to be at a generally acceptable threshold of willingness to pay.

In summary, the findings derived from the studies in this thesis support the efficacy of self-reported physical activity level for assessing risk and of physical activity on prescripton as a mean of improving the PA level of patients. While physical inactivity remains an important target for the healthcare system, the results from the present thesis may aid ongoing work in order to achieve an increased PA level in the population and among patients.

FUTURE PERSPECTIVES

The exploration of the possibilities of using a simple assessment tool in research is one thing. The next step would be to see how it could work in clinical practice. The measurement of physical activity behaviour is complicated and has been discusssed for many years. However, the main objective should be to improve the PA behaviour instead of focusing on which measure is most important. An interesting tentative comparative study would be to use either a CRF test or SGPALS assessment to analyse effect following PAP, and at clinical check-ups. Validation of these measures using an accelerometer would also be highly relevant.

Fitness tests have been shown to increase the precision of future cardiovascular risk estimation (69, 192). However, performing fitness test is time-consuming and quite expensive. Although submaximal fitness testing may be more accessible, an even simpler assessment tool associated with CRF could perhaps overcome this problem. It would certainly be of interest to add information about fitness and SGPALS to different scoring methods and analyse if the level of precision could be improved by adding SGPALS to, for example, SCORE (193).

Furthermore, it would be relevant to conduct an intervention in a working population using SGPALS to find physically inactive individuals and prescribe PAP in combination with assessment of physical activity behaviour. The goal would be to reduce mental health problems, improve HRQL and analyse its cost-effectiveness on a societal level.

In future studies, it might also be possible to determine how SGPALS could be used in a short-term follow-up using the three-month timeframe for self-assessed PA, in comparison to the one-year recall currently used in SGPALS.

Another perspective could be to explore how SGPALS could work as an assessment tool, used in conjunction with the summoning of patients for healthcare appointments. SGPALS could be used to discuss physical activity behaviour more extensively during clinical visits. This could possibly lead to behavioural change by mutual agreement. If SGPALS is to be included as 'a fifth vital sign' in clinical practice, it must be evaluated more extensively in different populations and age groups.

The Swedish healthcare system uses the PAP method, which is designed to increase physical activity behaviour. Different frameworks (variants of PAP), exist also on a national level. These could be further explored from a cost-effectiveness perspective. To identify, improve and refine the 'golden' PAP-method, further long-term follow-up studies and analyses are needed if graded initiation is to improve cost-effectiveness. Activities performed by the patients themselves, separate from the involvement of other third-party organisations, are probably cost-effective. Furthermore, adverse events have been reported in some studies and these require further investigation to improve potentially preventable accidents during physical activity. This could improve cost-effectiveness even further and support the decision-makers' willingness to pay for the PAP method.

In addition, international comparison of different methods designed for improved physical activity behaviour could also encourage decision-makers to support the most cost-effective method on a broader geographical scale.

ACKNOWLEDGEMENTS

I would like to express my gratitude and appreciation to all who, in one way or another, have contributed to this work. I thank you all, and especially:

Mats Börjesson, my main supervisor, who I met early as medical student. I still recollect our discussion regarding fitness and the correlation to the Norwegian football league during one of the first evenings at the emergency room at SU/Östra. Thank you, for your perpetuate patience and capacity to enlighten my path through this thesis.

Ingibjörg Jonsdottir, my co-supervisor, for always supporting my efforts to develop throughout the scientific context. Your ability to improve my ability has borne fruit.

Dag Thelle, my co-supervisor, for sharing your vast experience with me at times when needed.

Lena Björck, co-author, for sharing experiences and thoughts during early stages of the process.

Georgios Lappas, co-author, for your statistical advice and friendly considerateness.

Lars Hagberg, co-author, for sharing your knowledge in health economics.

Annika Rosengren, co-author, for inspiring lectures during medical school and later contributing to my development as a researcher.

Gunnar Grimby, co-author, for aiding the development of the SGPALS into its present form.

Gunnar Ahlborg Jr., co-author, for encouragement and all our discussions during my time at the Institute of Stress Medicine (ISM).

Marita Snällman, for the assistance with the Physical Activity on Prescription-study.

Eva Thydén, for administrative support during the process and with the layout of the thesis.

All friends and co-workers at the ISM. It has always been a haven for a stressed research student to work in your context. Especially *Emina Hadžibajramović* for statistical advice and *Anna-Karin Lennartsson* for help during the Physical Activity on Prescription-study.

Present and former bosses at the Department of Medicine at Halland Hospital Varberg, for supporting my efforts along the process, especially *Otto Überbacher, Görel Sundbeck, Marinko Dragic* and *Markus Lingman*.

All colleagues and personnel at the Department of Medicine at Halland Hospital Varberg, for your support and patience, especially *Ann-Kristin Nilsson* for help with computer issues, and all at the Endocrine section for your support.

Mona Huss Walin, for allowing me to use the litograph 'Brunnsgrävning i Humleskogen' in this and former research publications.

Håkan Hellström, for eloquent lyrics and music, -inspirational from the beginning to the end.

All friends and relatives, for your friendship and encouragement, especially *Per*, my brother, *Daniel Fornell* and *Carl Rohdén* for being such great friends at all times, *Per Jemsby* for improving my tennis and being a dual sounding board.

Ulla, my mother-in-law, for all the help and support, making the daily-life easier.

Birgitta and *Stig*, my parents, for love, everlasting trust and constant support. Also for showing me the possibilities with life and always encouraging me to walk my own path.

Sandra, my beloved wife, for endless love, support and everything. - My love - now - let us plan our decades to come!

Elias, Lovisa and ♂♥, for showing me that the presence is always present although very soon the past. I love you!

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